COMMENTS SUBMISSION: DOCKET 03D-0060

April 25, 2003
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Phase Forward appreciates the opportunity to review and comment on this 21CFR11 Guidance on Scope and Application. In general, the Guidance directly addresses some important issues for the industry, and is very proactive on the part of FDA. However, there are some areas that may need additional consideration. Our comments reflect our experience, and that of many of our customers, in the validation of enterprise software for Internet-based clinical data management.

Specific Comments

I. INTRODUCTION

Comment: It is recommended that the FDA state unequivocally that 21CFR11 is still in effect. There are varying opinions and discussions in the industry and by software suppliers as to the relevance of 21CFR11, and whether this guidance signifies a relaxing of the requirements of Part 11 by FDA.

III. A. Overall Approach to Part 11 Requirements

Comments:

The guidance states "we are now clarifying that fewer records will be considered subject to Part 11. It is recommended that this be expounded upon to provide additional understanding as to what the meaning and implication of "fewer records" is.

In the discussion section and throughout the guidance "enforcement discretion" is referred to without any clear definition of what it means. It is recommended that additional details or minimal guidelines be provided to facilitate a better understanding as to what "enforcement discretion" means to the inspectors in the field, and how this concept and/or guideline will be communicated to the field so it results in a consistent implementation and treatment of "enforcement discretion" during upcoming inspections. In addition, it is recommended that additional clarity be provided as to what "enforcement discretion" means with regard to validation, audit trails, and legacy systems specifically.

III. C.1. Overall Approach to Part 11 Requirements-Validation

Comments:

The statements contained in 198-210 give the impression that FDA no longer considers validation to be a requirement, and that there is no longer a strong emphasis on validation. It is recommended that a statement be included to emphasize that validation is required for systems that contain records under Part 11, but the extent of validation should be based on predicate rules, on a risk-based, science-based assessment, and on the potential of the system to affect product quality and safety and record integrity. LINE 212-The guidance references the Guidance for Industry and FDA staff *General Principles of Software Validation and GAMP 4 guide.* While these are excellent references for addressing validation and Part 11, the previous Part 11 guidance on validation provided much needed detail and direction as

to the basic elements FDA expects to be in place regarding Validation (i.eValidation Plan, Test Plan, Testing coverage, documentation deliverables and summaries etc.) It is recommended that the FDA consider inserting selected sections of this guidance into the current guidance to provide some basic elements and expectations regarding validation and Part 11.

III. C.2. Overall Approach to Part 11 Requirements-Audit Trail

Comments: The guidance states "Audit Trails are particularly important where the users are expected to create, modify, or delete regulated records during normal operation" This statement does not differentiate between a document or record and the data contained in the record. It is possible that only particular data contained within a record/document are required under the predicate rule. It recommended that the guidance differentiate between electronic records and the data contained in the record. Records would most likely relate to versions of a document, data would relate to modifications, changes or deletions to the data executed by an individual or individuals during normal operation.

III. C.3. Overall Approach to Part 11 Requirements-Legacy Systems

Comments: It recommended that additionally clarity be provided regarding the definition of Legacy System. While systems deployed prior to August 20, 1997 may have complied with all predicate rule requirements, and continue to be fit for their intended use, most likely significant changes have been made to the system over the past six years. It is recommended that a better understanding of acceptable changes to legacy systems be provided. What components are considered to be acceptable regarding software and hardware components while ensuring the system is compliant with predicate rule and its intended use.

III. C.4. Overall Approach to Part 11 Requirements-Copies of Records

Comments: There appears to be a contradiction regarding copies of electronic records. The guidance states "We recommend you supply copies of electronic records by: producing copies of records held in common portable formats…including PDF. Then the guidance goes on to state that if it is "technically feasible" …you should allow inspection…using your hardware, software, following your established procedures. The later statement would indicate that not only copies in a common portable format is required, but also a fully operational system for review of the electronic records. It is recommended that additional clarity be provided as to the requirements for copies of records.

III. C.5. Overall Approach to Part 11 Requirements-Record Retention

Comments: There appears to be a contradiction and an inconsistency regarding Record Retention of electronic records between the current guidance and the original guidance on Use of Computerized Systems in Clinical Trials. The current guidance indicates that maintaining records in a common portable format such as PDF is acceptable while the original guidance imposes requirements that include complete reconstruction of a study including hardware, software etc. These two approaches and guidelines are in direct contradiction with each other. It is recommended that additional clarity be provided that define the specific requirements with regard to record retention. In addition, it is recommended that the FDA provide further clarification as to the status of the Computerized Systems used in Clinical Trials guidance document and consider revising the document so that is more consistent with the approach and content of this current guidance.